

CLAIMS

1. A nucleic acid probe comprised of an n-meric nucleic acid comprising any number of 1 to n monomeric linked nucleic acid (LNA) moieties that may be situated in any position(s) of the nucleic acid sequence, wherein said nucleic acid probe is derivatized with at least one dye and wherein n is an integer selected from 1-200.
2. The nucleic acid probe of claim 1, wherein said probe is complementary or largely complementary to a section of a nucleic acid analyte comprising a single nucleotide polymorphism (SNP) site, wherein one monomeric LNA moiety is positioned opposite to the SNP site subsequent to the hybridization of the probe with the analyte.
3. The nucleic acid probe of claim 2 wherein said monomeric LNA moiety is complementary to the opposing SNP site of the nucleic acid analyte.
4. The nucleic acid probe of claim 2 wherein said monomeric LNA moiety is not complementary to the opposing SNP site of the nucleic acid analyte.
5. The nucleic acid probe of claim 1, wherein said probe is derivatized with two or more non-identical covalently attached dyes, wherein at least one of said dyes is a fluorescent dye.
6. The nucleic acid probe of claim 5, wherein said probe is comprised of a fluorescent dye and a non-fluorescent quencher dye.
7. The nucleic acid probe of claim 5, wherein said probe is comprised of two different fluorescent dyes, wherein said fluorescent dyes are able to jointly constitute the donor dye and the acceptor dye, respectively, of a FRET system.
8. A pair of nucleic acid probes comprised of either two nucleic acid probes of claim 1 or one nucleic acid probe of claim 1 and another nucleic acid probe that is derivatized with at least one dye, wherein both probes comprise nucleic acids having nucleotide sequences differing from each other, that are complementary or largely complementary to adjacent segments of the target sequence of the nucleic acid analyte, wherein the two probes are

collectively derivatized with two or more non-identical covalently attached dyes, wherein at least one dye is fluorescent, and wherein each probe comprises at least one of said dyes.

9. The pair of nucleic acid probes according to claim 8, comprising a fluorescent dye and a non-fluorescent quencher dye.

10. The pair of nucleic acid probes according to claim 8, comprising two fluorescent dyes, wherein said fluorescent dyes are able to jointly constitute the donor dye and the acceptor dye, respectively, of a FRET system.

11. A method for detection or quantification of a nucleic acid analyte comprising the steps of:

a.) providing a nucleic acid probe, wherein said nucleic acid probe is comprised of at least one monomeric LNA moiety and with two or more non-identical covalently attached dyes, wherein at least one dye is fluorescent;

b.) contacting said nucleic acid probe with the nucleic acid analyte so as to allow for the hybridization of the nucleic acid probe with the nucleic acid analyte; and

c.) measuring the change in the fluorescence of the nucleic acid probe that is related to the hybridization of the nucleic acid probe with the nucleic acid analyte.

12. The method of claim 11 wherein the nucleic acid probe comprises a fluorescent dye and a non-fluorescent quencher dye.

13. The method of claim 11 wherein the nucleic acid probe comprises a donor dye and an acceptor dye, respectively, which are able to jointly constitute a FRET system.

14. The method of claim 11 carried out as a homogeneous assay to detect or quantify a nucleic acid analyte in a sample.

15. The method of claim 11 wherein said change in the fluorescence occurs upon the hybridization of the nucleic acid probe with the nucleic acid analyte.

16. The method of claim 11 wherein said change in the fluorescence occurs upon the hydrolysis of the nucleic acid probe as hybridized with the nucleic acid analyte.

17. The method of claim 14 wherein the homogeneous assay is a polymerase chain reaction.

18. The method of claim 17 wherein said nucleic acid probe functions as a hybridization probe in a polymerase chain reaction, providing for a real-time detection or quantification of the amplification product.

19. The method of claim 11 wherein the nucleic acid probe is adapted for use as Molecular Beacon.

20. The method of claim 16 wherein the probe is hydrolyzed during the DNA synthesis steps of the temperature cycles of the polymerase chain reaction.

21. The method of claim 20 wherein the nucleic acid probe is adapted for the use as a Taqman probe.

22. The method of claim 11 conducted in a multiplexed format.

23. The method of claim 11 for analyzing a SNP site of a nucleic acid analyte, wherein said nucleic acid probe comprises a monomeric LNA moiety that is positioned opposite to the SNP site subsequent to the hybridization of the probe with the analyte.

24. A method for detection or quantification of a nucleic acid analyte comprising the steps of:

a.) providing a pair of nucleic acid probes, wherein said probes differ in their nucleic acid sequences, and wherein said probes collectively include at least one monomeric LNA moiety and are collectively derivatized with two or more non-identical covalently attached dyes, wherein at least one dye is fluorescent, and wherein the each probe comprises at least one of said dyes.

b.) contacting said pair of nucleic acid probes with the nucleic acid analyte so as to allow for the hybridization of the pair of nucleic acid probes with the nucleic acid analyte in such a way that both probes are hybridized to adjacent segments of the target sequence of the nucleic acid analyte; and

5 c.) measuring the change in the fluorescence of the pair of nucleic acid probes that is related to the hybridization of the nucleic acid probe with the nucleic acid analyte.

25. The method of claim 24 wherein the pair of nucleic acid probes comprises a fluorescent dye and a non-fluorescent quencher dye.

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26. The method of claim 24 wherein the pair of nucleic acid probes comprises a donor dye and an acceptor dye, respectively, which are able to jointly constitute a FRET system.

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27. The method of claim 26 wherein upon said hybridization of the pair of nucleic acid probes with the nucleic acid analyte the donor and the acceptor dyes are within 25 nucleotides of one another.

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28. The method of claim 27 wherein donor dye is fluorescein and the acceptor dye is Cy5 or Cy5.5.

29. The method of claim 27 wherein donor dye is fluorescein and the acceptor dye is LC Red 640 or LC Red 705.

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30. The method of claim 24 carried out as a homogeneous assay to detect or quantify a nucleic acid analyte in a sample.

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31. The method of claim 24 wherein said change in the fluorescence occurs upon the hybridization of both probes of the pair of nucleic acid probes with the nucleic acid analyte.

32. The method of claim 24 wherein said change in the fluorescence occurs upon the removal of at least one of the probes as hybridized with the nucleic acid analyte.

33. The method of claim 30 wherein the homogeneous assay is a polymerase chain reaction.

5 34. The method of claim 32 wherein at least one of the probes is removed during the DNA synthesis steps of the temperature cycles of the polymerase chain reaction.

10 35. The method of claim 33 wherein said pair of nucleic acid probes functions as a pair of hybridization probes in a polymerase chain reaction, providing for a real-time detection or quantification of the amplification product.

36. The method of claim 35 wherein the pair of nucleic acid probes is adapted for the use as LightCycler probes.

15 37. The method of claim 24 conducted in a multiplexed format.

38. The method of claim 24 for analyzing a SNP site of a nucleic acid analyte, wherein said pair of nucleic acid probes comprises a monomeric LNA moiety that is positioned opposite to the SNP site subsequent to the hybridization of the probes with the analyte.